SEQUENCE LISTING

<110	SI We SI Po	heets ells hell oorma	, Yos s, M , Pe y, Jo an, l Den	ichae ter i ohn i Roge:	el P A. A. r A.												
<120			ntin vity		-Read	d As	say :	for	the 1	Dete	ctio	n of	De 1	Novo	HCV	RNA	Polymerase
<130	> (02-3	33-A														
<160	> '	7															
<170	>]	Pate	ntIn	ver	sion	3.1											
<210> 1 <211> 1803 <212> DNA <213> Hepatitis C virus																	
<220> <221> CDS <222> (1)(1803) <223>																	
<400		_															
atg (Met)	Ala	ser	Met	Ser 5	Met	Ser	Tyr	aca Thr	tgg Trp 10	aca Thr	ggc Gly	gcc Ala	ctg Leu	atc Ile 15	aca Thr		48
ccg Pro																	96
tcc : Ser :	ttg Leu	ctg Leu 35	cgt Arg	cac His	cat His	aac Asn	ctg Leu 40	gtc Val	tat Tyr	tcc Ser	aca Thr	aca Thr 45	tcc Ser	cgc Arg	agt Ser		144
gca a Ala																	192
gac g Asp 7	gat Asp	cat His	tac Tyr	cgg Arg	gac Asp 70	gtg Val	ctc Leu	aag Lys	gag Glu	atg Met 75	aag Lys	gcg Ala	aag Lys	gcg Ala	tcc Ser 80		240
aca q	gtg Val	aag Lys	gct Ala	aaa Lys 85	ctg Leu	cta Leu	tct Ser	gta Val	gaa Glu 90	gaa Glu	gca Ala	tgc Cys	aag Lys	ctg Leu 95	acg Thr		288
ccc o	ccg Pro	cat His	tcg Ser 100	gcc Ala	aaa Lys	tcc Ser	aaa Lys	ttt Phe 105	ggc Gly	tat Tyr	gly aaa	gca Ala	aag Lys 110	gac Asp	gtc Val		336

		cta Leu 115														384
		ctg Leu														432
		gag Glu														480
		ctc Leu														528
		ctt Leu														576
		tac Tyr 195														624
		acc Thr														672
acc Thr 225	cgc Arg	tgt Cys	ttt Phe	gac Asp	tca Ser 230	acg Thr	gtc Val	act Thr	gag Glu	aat Asn 235	gac Asp	atc Ile	cgt Arg	gtt Val	gag Glu 240	720
gag Glu	tca Ser	att Ile	tac Tyr	caa Gln 245	tgt Cys	tgt Cys	gac Asp	ttg Leu	gcc Ala 250	ccc Pro	gaa Glu	gct Ala	aga Arg	cag Gln 255	gcc Ala	768
		tcg Ser														816
tcc Ser	aaa Lys	999 Gly 275	cag Gln	aac Asn	tgc Cys	ggc Gly	tat Tyr 280	cgc Arg	cgg Arg	tgc Cys	cgc Arg	gcg Ala 285	agc Ser	ggc Gly	gtg Val	864
ctg Leu	acg Thr 290	act Thr	agc Ser	tgc Cys	ggt Gly	aat Asn 295	acc Thr	ctc Leu	aca Thr	tgc Cys	tac Tyr 300	ttg Leu	aag Lys	gcc Ala	gct Ala	912
		tgt Cys														960
gga Gly	gac Asp	gac Asp	ctt Leu	gtc Val 325	gtt Val	atc Ile	tgt Cys	gaa Glu	agc Ser 330	gcg Ala	gga Gly	acc Thr	caa Gln	gag Glu 335	gac Asp	1008
gcg	gca	agc	cta	cga	gtc	ttc	acg	gag	gct	atg	act	agg	tac	tct	gcc	1056

Ala	Ala	Ser	Leu 340	Arg	Val	Phe	Thr	Glu 345	Ala	Met	Thr	Arg	Tyr 350	Ser	Ala	
					ccc Pro											1104
					gtg Val											1152
					cgt Arg 390											1200
					cac His											1248
					act Thr											1296
					cta Leu											1344
					gct Ala											1392
					ctc Leu 470											1440
tac Tyr	tct Ser	cca Pro	ggt Gly	gag Glu 485	atc Ile	aat Asn	agg Arg	gtg Val	gct Ala 490	tca Ser	tgc Cys	ctc Leu	agg Arg	aag Lys 495	ctt Leu	1488
					cga Arg											1536
					cag Gln											1584
					gta Val											1632
					gac Asp 550											1680
gly ggg	gga Gly	gac Asp	ata Ile	tat Tyr	cac His	agc Ser	ctg Leu	tct Ser	cgt Arg	gcc Ala	cga Arg	ccc Pro	cgc Arg	tgg Trp	ttc Phe	1728

565 570 575

1803

atg ttg tgc cta ctc cta ctc tcc gta ggg gta ggc atc tat cta ctc 1776

Met Leu Cys Leu Leu Leu Ser Val Gly Val Gly Ile Tyr Leu Leu

580

585

590

580 585 590

ccc aac cgg cat cac cat cac cat cac
Pro Asn Arg His His His His His
595 600

<210> 2

<211> 601

<212> PRT

<213> Hepatitis C virus

<400> 2

Met Ala Ser Met Ser Met Ser Tyr Thr Trp Thr Gly Ala Leu Ile Thr 1 5 10 15

Pro Cys Ala Ala Glu Glu Ser Lys Leu Pro Ile Asn Ala Leu Ser Asn 20 25 30

Ser Leu Leu Arg His His Asn Leu Val Tyr Ser Thr Thr Ser Arg Ser 35 40 45

Ala Ser Leu Arg Gln Lys Lys Val Thr Phe Asp Arg Leu Gln Val Leu 50 55 60

Asp Asp His Tyr Arg Asp Val Leu Lys Glu Met Lys Ala Lys Ala Ser 70 75 80

Thr Val Lys Ala Lys Leu Leu Ser Val Glu Glu Ala Cys Lys Leu Thr 85 90 95

Pro Pro His Ser Ala Lys Ser Lys Phe Gly Tyr Gly Ala Lys Asp Val

Arg Ser Leu Ser Ser Arg Ala Val Asn His Ile Arg Ser Val Trp Lys 115 120 125

Asp Leu Leu Glu Asp Thr Asp Thr Pro Ile Gln Thr Thr Ile Met Ala 130 135 140

Lys Asn Glu Val Phe Cys Val Gln Pro Glu Lys Gly Gly Arg Lys Pro 145 150 155 160 Ala Arg Leu Ile Val Phe Pro Asp Leu Gly Val Arg Val Cys Glu Lys 165 170 175

Met Ala Leu Tyr Asp Val Val Ser Thr Leu Pro Gln Ala Val Met Gly

185

Ser Ser Tyr Gly Phe Gln Tyr Ser Pro Lys Gln Arg Val Glu Phe Leu 195 200 205

Val Asn Thr Trp Lys Ala Lys Lys Cys Pro Met Gly Phe Ser Tyr Asp 210 215 220

Thr Arg Cys Phe Asp Ser Thr Val Thr Glu Asn Asp Ile Arg Val Glu 225 230 235 . 240

Glu Ser Ile Tyr Gln Cys Cys Asp Leu Ala Pro Glu Ala Arg Gln Ala 245 250 255

Ile Arg Ser Leu Thr Glu Arg Leu Tyr Val Gly Gly Pro Met Thr Asn 260 265 270

Ser Lys Gly Gln Asn Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val 275 280 285

Leu Thr Thr Ser Cys Gly Asn Thr Leu Thr Cys Tyr Leu Lys Ala Ala 290 295 300

Ala Ala Cys Arg Ala Ala Lys Leu Gln Asp Cys Thr Met Leu Val Asn 305 310 315

Gly Asp Asp Leu Val Val Ile Cys Glu Ser Ala Gly Thr Gln Glu Asp 325 330 335

Ala Ala Ser Leu Arg Val Phe Thr Glu Ala Met Thr Arg Tyr Ser Ala 340 345 350

Pro Pro Gly Asp Pro Pro Gln Pro Glu Tyr Asp Leu Glu Leu Ile Thr 355 360 365

Ser Cys Ser Ser Asn Val Ser Val Ala His Asp Ala Ser Gly Lys Arg 370 380

Val Tyr Tyr Leu Thr Arg Asp Pro Thr Val Pro Leu Ala Arg Ala Ala 385 390 395 400

Trp Glu Thr Ala Arg His Thr Pro Val Asn Ser Trp Leu Gly Asn Ile 405 410 415

Ile Met Tyr Ala Pro Thr Leu Trp Ala Arg Met Ile Leu Met Thr His 420 425 430

Phe Phe Ser Ile Leu Leu Ala Gln Glu Gln Leu Glu Lys Ala Leu Asp 435 440 445

Cys Gln Ile Tyr Gly Ala Cys Tyr Ser Ile Glu Pro Leu Asp Leu Pro 450 455 460

Gln Ile Ile Glu Arg Leu His Gly Leu Ser Ala Phe Ser Leu His Ser 465 470 475 480

Tyr Ser Pro Gly Glu Ile Asn Arg Val Ala Ser Cys Leu Arg Lys Leu 485 490 495

Gly Val Pro Pro Leu Arg Val Trp Arg His Arg Ala Arg Ser Val Arg 500 505 510

Ala Lys Leu Leu Ser Gln Gly Gly Arg Ala Ile Cys Gly Lys Tyr 515 520 525

Leu Phe Asn Trp Ala Val Arg Thr Lys Leu Lys Leu Thr Pro Ile Pro 530 540

Ala Ala Ser Arg Leu Asp Leu Ser Gly Trp Phe Val Ala Gly Tyr Ser 545 550 555 560

Gly Gly Asp Ile Tyr His Ser Leu Ser Arg Ala Arg Pro Arg Trp Phe 565 570 575

Met Leu Cys Leu Leu Leu Ser Val Gly Val Gly Ile Tyr Leu Leu 580 585 590

Pro Asn Arg His His His His His 595 600

<210> 3

```
<211> 1740
<212>
       DNA
<213>
       Artificial
<220>
<223>
       C-terminally truncated HCV NS5B polymerase (C delta 21 NS5B)
<220>
<221>
      CDS
<222>
       (1)..(1740)
<223>
<400> 3
atg get age atg tea atg tee tat aca tgg aca gge gee etg ate aca
                                                                       48
Met Ala Ser Met Ser Met Ser Tyr Thr Trp Thr Gly Ala Leu Ile Thr
ccg tgc gct gcg gag gaa agc aaq ctq ccc atc aac qcq ctq aqc aac
                                                                       96
Pro Cys Ala Ala Glu Glu Ser Lys Leu Pro Ile Asn Ala Leu Ser Asn
                                 25
tcc ttg ctg cgt cac cat aac ctg gtc tat tcc aca aca tcc cgc agt
                                                                      144
Ser Leu Leu Arg His His Asn Leu Val Tyr Ser Thr Thr Ser Arg Ser
gca agc ctg cgg cag aag gtc acc ttt gac aga ctg caa gtc ctg
                                                                      192
Ala Ser Leu Arg Gln Lys Lys Val Thr Phe Asp Arg Leu Gln Val Leu
    50
                        55
gac gat cat tac cgg gac gtg ctc aag gag atg aag gcg aag gcg tcc
                                                                      240
Asp Asp His Tyr Arg Asp Val Leu Lys Glu Met Lys Ala Lys Ala Ser
                    70
aca gtg aag gct aaa ctg cta tct gta gaa gaa gca tgc aag ctg acg
                                                                      288
Thr Val Lys Ala Lys Leu Leu Ser Val Glu Glu Ala Cys Lys Leu Thr
ccc ccg cat tcg gcc aaa tcc aaa ttt ggc tat ggg gca aag gac gtc
                                                                      336
Pro Pro His Ser Ala Lys Ser Lys Phe Gly Tyr Gly Ala Lys Asp Val
cgg agc cta tcc agc agg gcc gtt aac cac atc cgc tcc gtg tgg aag
                                                                      384
Arg Ser Leu Ser Ser Arg Ala Val Asn His Ile Arg Ser Val Trp Lys
        115
                            120
                                                 125
gac ttg ctg gag gac act gac aca cca att cag acc acc atc atg gca
                                                                      432
Asp Leu Leu Glu Asp Thr Asp Thr Pro Ile Gln Thr Thr Ile Met Ala
    130
                        135
                                             140
aaa aat gag gtt ttc tgc gtc caa cca gag aaa gga ggc cgc aaa cca
                                                                      480
Lys Asn Glu Val Phe Cys Val Gln Pro Glu Lys Gly Gly Arg Lys Pro
145
                    150
                                         155
gct cgc ctc atc gta ttc cca gac ctg gga gtt cgt gta tgc gag aag
                                                                      528
Ala Arg Leu Ile Val Phe Pro Asp Leu Gly Val Arg Val Cys Glu Lys
                165
                                    170
```

					gtg Val											576
					caa Gln											624
					gca Ala											672
					tca Ser 230											720
gag Glu	tca Ser	att Ile	tac Tyr	caa Gln 245	tgt Cys	tgt Cys	gac Asp	ttg Leu	gcc Ala 250	ccc Pro	gaa Glu	gct Ala	aga Arg	cag Gln 255	gcc Ala	768
ata Ile	agg Arg	tcg Ser	ctc Leu 260	aca Thr	gag Glu	cgg Arg	ctc Leu	tat Tyr 265	gtc Val	Gly aaa	ggt Gly	ccc Pro	atg Met 270	act Thr	aac Asn	816
tcc Ser	aaa Lys	ggg Gly 275	cag Gln	aac Asn	tgc Cys	ggc Gly	tat Tyr 280	cgc Arg	cgg Arg	tgc Cys	cgc Arg	gcg Ala 285	agc Ser	ggc Gly	gtg Val	864
ctg Leu	acg Thr 290	act Thr	agc Ser	tgc Cys	ggt Gly	aat Asn 295	acc Thr	ctc Leu	aca Thr	tgc Cys	tac Tyr 300	ttg Leu	aag Lys	gcc Ala	gct Ala	912
gca Ala 305	gcc Ala	tgt Cys	cga Arg	gct Ala	gcc Ala 310	aag Lys	ctc Leu	cag Gln	gac Asp	tgc Cys 315	acg Thr	atg Met	ctc Leu	gtg Val	aat Asn 320	960
gga Gly	gac Asp	gac Asp	ctt Leu	gtc Val 325	gtt Val	atc Ile	tgt Cys	gaa Glu	agc Ser 330	gcg Ala	gga Gly	acc Thr	caa Gln	gag Glu 335	gac Asp	1008
gcg Ala	gca Ala	agc Ser	cta Leu 340	cga Arg	gtc Val	ttc Phe	acg Thr	gag Glu 345	gct Ala	atg Met	act Thr	agg Arg	tac Tyr 350	tct Ser	gcc Ala	1056
ccc Pro	cct Pro	ggg Gly 355	gac Asp	ccg Pro	ccc Pro	caa Gln	ccg Pro 360	gaa Glu	tac Tyr	gac Asp	ttg Leu	gag Glu 365	ctg Leu	ata Ile	aca Thr	1104
tcg Ser	tgt Cys 370	tcc Ser	tcc Ser	aat Asn	gtg Val	tcg Ser 375	gtc Val	gca Ala	cac His	gat Asp	gca Ala 380	tct Ser	ggc Gly	aaa Lys	agg Arg	1152
gtg Val 385	tac Tyr	tac Tyr	ctc Leu	acc Thr	cgt Arg 390	gac Asp	ccc Pro	acc Thr	gtc Val	ccc Pro 395	ctt Leu	gcg Ala	cgg Arg	gct Ala	gcg Ala 400	1200
tgg	gag	aca	gct	agg	cac	act	cca	gtc	aac	tcc	tgg	cta	ggc	aac	atc	1248

Trp Gl	u Thr	Ala	Arg 405	His	Thr	Pro	Val	Asn 410	Ser	Trp	Leu	Gly	Asn 415	Ile	
atc at Ile Me															1296
ttc tt Phe Ph															1344
tgt ca Cys Gl 45	n Ile														1392
cag at Gln Il 465															1440
tac tc Tyr Se	t cca r Pro	ggt Gly	gag Glu 485	atc Ile	aat Asn	agg Arg	gtg Val	gct Ala 490	tca Ser	tgc Cys	ctc Leu	agg Arg	aag Lys 495	ctt Leu	1488
ggg gt Gly Va															1536
gct aa Ala Ly	g tta s Leu 515	ctg Leu	tcc Ser	cag Gln	ggg Gly	999 Gly 520	agg Arg	gcc Ala	gcc Ala	att Ile	tgt Cys 525	ggc Gly	aag Lys	tac Tyr	1584
ctc tt Leu Ph 53	e Asn														1632
gct gc Ala Al 545	g tcc a Ser	cgg Arg	ctg Leu	gac Asp 550	ttg Leu	tcc Ser	ggc Gly	tgg Trp	ttc Phe 555	gtt Val	gct Ala	ggc Gly	tac Tyr	agc Ser 560	1680
GJÀ GJ aaa aa	a gac y Asp	ata Ile	tat Tyr 565	cac His	agc Ser	ctg Leu	tct Ser	cgt Arg 570	gcc Ala	cga Arg	ccc Pro	cgc Arg	cat His 575	cac His	1728
cat ca His Hi															1740
	4 580 PRT Arti	ficia	al												
<220> <223>	C-te	rmina	ally	trur	ıcate	ed HC	V NS	85B p	olym	neras	se (C	c del	ta 2	1 NS5B)	
<400>	4		-					•	•				_	,	

Met Ala Ser Met Ser Met Ser Tyr Thr Trp Thr Gly Ala Leu Ile Thr 1 5 10 15

Pro Cys Ala Ala Glu Glu Ser Lys Leu Pro Ile Asn Ala Leu Ser Asn 20 25 30

Ser Leu Leu Arg His His Asn Leu Val Tyr Ser Thr Thr Ser Arg Ser 35 40 45

Ala Ser Leu Arg Gln Lys Lys Val Thr Phe Asp Arg Leu Gln Val Leu 50 55 60

Asp Asp His Tyr Arg Asp Val Leu Lys Glu Met Lys Ala Lys Ala Ser 65 70 75 80

Thr Val Lys Ala Lys Leu Leu Ser Val Glu Glu Ala Cys Lys Leu Thr 85 90 95

Pro Pro His Ser Ala Lys Ser Lys Phe Gly Tyr Gly Ala Lys Asp Val 100 105 110

Arg Ser Leu Ser Ser Arg Ala Val Asn His Ile Arg Ser Val Trp Lys
115 120 125

Asp Leu Leu Glu Asp Thr Asp Thr Pro Ile Gln Thr Thr Ile Met Ala 130 135 140

Lys Asn Glu Val Phe Cys Val Gln Pro Glu Lys Gly Gly Arg Lys Pro 145 150 155 160

Ala Arg Leu Ile Val Phe Pro Asp Leu Gly Val Arg Val Cys Glu Lys
165 170 175

Met Ala Leu Tyr Asp Val Val Ser Thr Leu Pro Gln Ala Val Met Gly 180 185 190

Ser Ser Tyr Gly Phe Gln Tyr Ser Pro Lys Gln Arg Val Glu Phe Leu 195 200 205

Val Asn Thr Trp Lys Ala Lys Lys Cys Pro Met Gly Phe Ser Tyr Asp 210 215 220

Thr Arg Cys Phe Asp Ser Thr Val Thr Glu Asn Asp Ile Arg Val Glu Glu Ser Ile Tyr Gln Cys Cys Asp Leu Ala Pro Glu Ala Arg Gln Ala Ile Arg Ser Leu Thr Glu Arg Leu Tyr Val Gly Pro Met Thr Asn Ser Lys Gly Gln Asn Cys Gly Tyr Arg Arg Cys Arg Ala Ser Gly Val Leu Thr Thr Ser Cys Gly Asn Thr Leu Thr Cys Tyr Leu Lys Ala Ala Ala Ala Cys Arg Ala Ala Lys Leu Gln Asp Cys Thr Met Leu Val Asn Gly Asp Asp Leu Val Val Ile Cys Glu Ser Ala Gly Thr Gln Glu Asp Ala Ala Ser Leu Arg Val Phe Thr Glu Ala Met Thr Arg Tyr Ser Ala Pro Pro Gly Asp Pro Pro Gln Pro Glu Tyr Asp Leu Glu Leu Ile Thr Ser Cys Ser Ser Asn Val Ser Val Ala His Asp Ala Ser Gly Lys Arg Val Tyr Tyr Leu Thr Arg Asp Pro Thr Val Pro Leu Ala Arg Ala Ala Trp Glu Thr Ala Arg His Thr Pro Val Asn Ser Trp Leu Gly Asn Ile Ile Met Tyr Ala Pro Thr Leu Trp Ala Arg Met Ile Leu Met Thr His

)

Cys Gln Ile Tyr Gly Ala Cys Tyr Ser Ile Glu Pro Leu Asp Leu Pro

Phe Phe Ser Ile Leu Leu Ala Gln Glu Gln Leu Glu Lys Ala Leu Asp

450 455 460

Gln Ile Ile Glu Arg Leu His Gly Leu Ser Ala Phe Ser Leu His Ser 465 470 475 480

Tyr Ser Pro Gly Glu Ile Asn Arg Val Ala Ser Cys Leu Arg Lys Leu 485 490 495

Gly Val Pro Pro Leu Arg Val Trp Arg His Arg Ala Arg Ser Val Arg 500 505 510

Ala Lys Leu Leu Ser Gln Gly Gly Arg Ala Ala Ile Cys Gly Lys Tyr 515 520 525

Leu Phe Asn Trp Ala Val Arg Thr Lys Leu Lys Leu Thr Pro Ile Pro 530 540

Ala Ala Ser Arg Leu Asp Leu Ser Gly Trp Phe Val Ala Gly Tyr Ser 545 550 555 560

Gly Gly Asp Ile Tyr His Ser Leu Ser Arg Ala Arg Pro Arg His His 565 570 575

His His His His 580

<210> 5

<211> 31

<212> RNA

<213> Artificial

<220>

<223> HCV NS5B polymerase oligonucleotide template

<400> 5

cgauacuccc uuuauauaac caucaaucgc c

31

<210> 6

<211> 32

<212> RNA

<213> Artificial

<220>

<223> HCV NS5B polymerase oligonucleotide template

<400> 6

cgauacuccc uuuauauaac caucaaucgc cc

32

<210> 7
<211> 46
<212> RNA
<213> Artificial

<220>
<223> HCV NS5B polymerase oligonucleotide template

<400> 7
cucauacgau acucacucua uauaacaauc aaucgcccu uucccc

O

46